the Examiner found Groups I and II to be distinct. MPEP 802.01 provides the following definition of "distinct":

> "The term "distinct" means that two or more subjects as disclosed are related, for example, as combination and part (subcombination) thereof, process and apparatus for its practice, process and product made, etc., but are capable of separate manufacture, use, or sale as claimed, AND ARE PATENTABLE (novel and unobvious) OVER EACH OTHER (though they may each be unpatentable because of the prior art)."

Thus, the Examiner's holding of Groups I and II as being distinct means the Examiner has found (at least implicitly) that Groups I and II as claimed are patentable over each other.

The Examiner first rejected claims 1-20 under 35 U.S.C. 112, second paragraph as being indefinite for failing to recite a final process step which agrees back with the preamble. Claim 20 has been canceled. Claims 1 and 18 (the only remaining independent claims) have been amended to add a final paragraph which now references fabricating the array. Hence, this rejection should now be withdrawn.

The Examiner next rejected claim 7 on the basis of use of the "the drive". Claim 7 (and claim 8) have been amended to refer to "the corrected drive pattern". Consequently, it is believed this rejection should now be withdrawn. As an aside, the Examiner states that a position encoder is used in reference to claim 7. However, Applicant does not see that such an element is recited in claim 7.

The Examiner next rejected claims 15 and 16 for lack of antecedent basis in relation to use of "<u>the</u> accuracy...". Claims 15 and 16 have been amended to now refer to "<u>an</u> accuracy...".

Turning now to the art rejections, the Examiner first rejected claims 1-19 under 35 U.S.C. 103(a) (note that claim 20 has been canceled and the rejection of that claim is therefore not discussed). In rejecting claims 1-19 the Examiner relied upon Budach et al. (Anal. Chem., 1991, *71*, 3347-3355) in combination with Suzuki (US 4,675,696). Note that in the initial portion of the rejection the Examiner refers to "Blanchard et al. (Biosensors and Bioelectronics 11, 687-690, 1996)" although that reference was never discussed. The Examiner confirmed in a telephone message to

me on Jan. 1/01 in response to my inquiry, that in fact the reference to Blanchard et al. should have been to the cited and relied upon Budach et al.

The above art rejection is discussed in relation to the identified claims below. Claims 1-19 are discussed first while additional reasons for the withdrawal in relation to some of the other identified claims are also presented.

Claims 1-19

In combining Budach et al. with Suzuki, the Examiner referred to page 3348, column 1, paragraphs 2 and 3, and the last paragraph of *Spot-to-Spot Reproducibility* in Budach et al. as a recognition of "resolution-type problems associated with ink jet deposition apparatus" used in forming oligonucleotide arrays. The Examiner then goes on to say that it would have been obvious to use the error correction of Suzuki with the oligonucleotide deposition method of Budach et al. This rejection is respectfully traversed on the basis that the Examiner has not established any suggestion or motivation from the references to make the combination proposed by the Examiner and that, if anything, the references actually teach away from any such combination. In particular, Budach et al. actually only use a single jet. This is pointed out on p. 3348, first column, first line of the second full paragraph:

> "The single-channel ink jet printer used in the present study..."

This is also referenced on p. 3349, first column, first sentence under the title "Ink-Jet Immobilization":

> "A single-channel ink-jet printer (Microdrop GmbH, Norderstedt, Germany) was used for the patterned immobilization of the capture probes. The ink-jet nozzle was coupled to a 1mL reservoir for the working solution. The ink-jet nozzle and reservoir were washed with 2-propanol and deionized water prior to filling with the working solution."

Additionally, enclosed is a copy of each of the following three pages downloaded from Microdrop GmbH on Jan.1/01:

(i) http://www.microdrop.de/html/contacts.html;
(ii) http://www.microdrop.de/html/products.html; and

(iii) http://www.microdrop.de/html/dispenser_heads.html.

Budach et al. itself, as well as particularly item (iii), make it clear that the type of dispenser used in Budach et al. was indeed a single jet dispenser.

Thus, while Budach et al. suggest that multiple jets could be used (see last sentence of the second full paragraph, column 1, p. 3348 - referenced by the Examiner) with potential problems described therein, they in fact only use a single jet. It is in this context that the discussion under *Spot-to-Spot Reproducibility* must be understood. In particular, Budach et al. notes that there is a spot-to-spot reproducibility problem. However, since he is only using one jet such spot-to-spot reproducibility is likely spot size variations (note they also refer to this as "inhomogeneous immobilization" - last sentence, first full paragraph, second column on p. 3354). <u>In any event, there is simply no suggestion that this "reproducibility" problem in Budach et al. was an error in relative positions of multiple jets since multiple jets or their problems were never investigated (nor discussed in relation to spot-to-spot reproducibility).</u> On the other hand, Suzuki is solely concerned with relative positions of multiple the recording jets. This is made clear in <u>many</u> portions of that reference. For <u>example</u>:

> Column 1, lines 17-18: "Consequently an aberration in the relative positioning of plural recording means, or of plural images recorded by said recording means, will lead to..."
>
> Column 1, lines 37-40: "An object of the present invention is to provide a recording apparatus not associated with the above-mentioned drawbacks..."
>
> Column 4, lines 65-66: "FIG. 4 is a view of a reference pattern for detecting relative positional aberration of the recording means". See also the remainder of the FIG. descriptions (e.g. FIGS. 6 and 7) in relation to detecting the "relative positional aberration".
>
> Column 3, lines 35-36: "The information on the relative positional aberration of the reference patterns..."
>
> Column 6, lines 15-16: Also the sensor utilized for detecting the relative positional aberrations of the nozzle heads..."

Again, the above are only <u>examples</u> of portions of Suzuki dealing with relative positioning errors in multiple ink dispensers. If the Examiner is of the view that

Suzuki teaches or suggests anything other than correcting for <u>relative</u> errors in the ink dispensers, he is respectfully requested to identify which portion(s) of Suzuki are relied upon for this teaching.

Thus, while Budach et al. teaches spot-to-spot reproducibility errors (most likely spot size) within a single dispenser, one of ordinary skill would not turn to Suzuki to try to correct this problem since Suzuki deals with an entirely different problem (solely with relative positional errors in multiple ink dispensers). Thus, there is no suggestion from the references to somehow try to combine them and if anything, one of ordinary skill would in fact be led to dismiss Suzuki (dealing with relative positional errors from multiple dispensers) as irrelevant to the problem described in Budach et al. (a problem which originates within a single dispenser itself).

In view of the above, the rejection of claims 1-19 based on Budach et al. in view of Suzuki should be withdrawn.

<u>Claims 5, 11, 19</u>

Claims 5, 11 additionally refer to the corrected drive pattern being saved in the memory. The Examiner has not pointed to any such feature in the references and consequently for this additional reason, the rejection of claim 5 should be withdrawn.

<u>Claim 13</u>

Claim 13 additionally refers to the operating parameter being the position of the substrate (note that the "operating parameter" is examined as per claim 1: "examining at least one operating parameter for an error from a nominal value"). While Suzuki deals with errors relative positions of ink dispensers, the Examiner has not pointed to anything in Suzuki or elsewhere suggesting the occurrence of an error in substrate position (which would affect the position of all deposited drops) or the generation of a corrected drive pattern based upon such a detected error. Accordingly, for this additional reason the rejection of claim 54 should be withdrawn.

<u>Claim 15, 52</u>

Claims 15, 52 additionally recites that the apparatus further includes a position encoder to detect the position of the dispensing head or the substrate, and that the at

least one parameter is an accuracy of the encoder. The Examiner has not pointed to any suggestion in the cited references of the use of an encoder in fabricating a biopolymer array nor how one would examine the encoder accuracy nor derive, based on such error, a corrected drive pattern (see the claim 1 language regarding use of the parameter). For this additional reason, the rejection of claim 15 should be withdrawn and claim 52 also allowed.

Claims 16, 46, 48

These claims additionally refer to the operating parameter being the accuracy in an ability of the transport system to move the substrate to an expected location in response to a command. Suzuki deals with correcting relative mis-positioning of different jets on a carriage 1 (see FIG. 1). However, the Examiner has not pointed to anything in Suzuki or the other cited references suggesting how an error in the transport system would be detected or the generation of a corrected drive pattern based upon such a detected error. Note that Suzuki's method dealing with relative mis-positions of the jets, would not even detect an error in the transport system far less correct for it.

Note that claim 48 specifically limits the operating parameter to an accuracy in an ability of the transport system to move the substrate to an expected location.

For this additional reason, the rejection of claim 16 should be withdrawn and claims 46, 48 also allowed.

Claim 47

New claim 47 refers to the at least one operating parameter being a deviation of actual movement of the substrate or head from a corresponding nominal axis of movement. This is supported, for example, by page 4, lines 28-29 and page 13, lines 20-21. Detecting such a deviation nor generating a corrected drive pattern based upon it, is not disclosed nor suggested in Budach et al. nor Suzuki. For this additional reason, the claim 47 should also be allowed.

Claim 49

New claim 49 additionally recites the operating parameter being a fluid volume dispensed by the deposition apparatus. This is supported, for example, by page 15, lines 16-17 and 22-29. Neither detecting such an error nor generating a corrected drive pattern based upon it, are disclosed or suggested in Budach et al. nor Suzuki. For this additional reason, claim 49 should also be allowed.

Claim 50

New claim 50 additionally recites that the operating parameter is an effect of thermal expansion. This is supported, for example, by page 13, lines 19-23 and page 14 lines 8-13. Neither detecting such an error nor generating a corrected drive pattern based upon it, are disclosed or suggested in Budach et al. nor Suzuki. For this additional reason, claim 50 should also be allowed.

Claim 52

New claim 52 is similar to claim 10 but is limited to where the operating parameter is the position of the dispensing head, or orientation of a nozzle, and is examined by viewing the dispensing head, or nozzle. Viewing the dispensing head or nozzle to detect the recited error and generating a corrected drive pattern based upon an error detected by this technique, are not disclosed nor suggested in Budach et al. nor Suzuki. For this additional reason, claim 52 should also be allowed.

Claims 53, 54

New claims 53 additionally recite that the positional error is a dynamic positional error. Correct positioning as referred to in the present application, can be static (i.e. fixed) or dynamic (i.e. changing, such as having a different magnitude at different positions of the head). This is disclosed, for example, on page 15, line 13. The positional errors in Suzuki are static (i.e. they do not vary depending upon the position of carriage 1). Accordingly, claims 53 and 54 should also be allowed for this additional reason.

Claim 55

New claim 55 additionally recites that the deposition apparatus comprises multiple jets for dispensing droplets, and wherein the corrected drive pattern comprises an instruction to switch to a different jet when a deviation from nominal volume is encountered for one jet which is more than a predetermined tolerance. Such a feature is disclosed, for example, on page 15, lines 26-29 and is not disclosed nor suggested by the cited Budach et al. or Suzuki references.

Conclusion

In view of the above amendments and discussion, claims 1-19 and 46-55 should now be in condition for allowance. If the Examiner is of the view that there are any outstanding issues, he is invited to call Gordon Stewart at (650)485-2386.

Respectfully submitted,

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APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (AMENDED) A method of fabricating an addressable array of biopolymer probes on a substrate according to a target array pattern using a deposition apparatus which, when operated according to a target drive pattern based on nominal operating parameters of the apparatus, provides the probes on the substrate in the target array pattern, the method comprising:
(a) examining at least one operating parameter for an error from a nominal value which error will result in use of the target drive pattern producing a discrepancy between the target array pattern and an actual array pattern deposited;
(b) when an error is detected deriving, based on the error, a corrected drive pattern different from the target drive pattern such that use of the corrected drive pattern results in a reduced discrepancy between the target and actual array patterns; and
(c) operating the deposition apparatus according to the corrected drive pattern so as to fabricate the array.

2. A method according to claim 1, additionally comprising operating the deposition apparatus according to the corrected drive pattern.

3. A method according to claim 1 wherein the probes are DNA or RNA probes.

4. A method according to claim 1 additionally comprising saving the target drive pattern in a memory of the deposition apparatus.

5. A method according to claim 1 additionally comprising saving the target drive pattern in a memory of the deposition apparatus, and wherein the corrected drive pattern is saved in the memory.

6. A method according to claim 1 wherein the corrected drive pattern is derived without obtaining a target drive pattern.

7. (AMENDED) A method according to claim 4 wherein:

the deposition apparatus includes a dispensing head to dispense fluid droplets containing the probes or probe precursors, and a transport system to move at least one of the dispensing head and substrate relative to the other as the droplets are dispensed from the head, so as to form the array; and

the corrected drive pattern controls operation of the transport system.

8. (AMENDED) A method according to claim 1 wherein:

the deposition apparatus includes a dispensing head to dispense fluid droplets containing the probes or probe precursors, and a transport system to move at least one of the dispensing head and substrate relative to the other as the droplets are dispensed from the head, so as to form the array;

the target drive pattern controls operation of the transport system; and

the operating parameter is the position of the substrate or dispensing head, which is examined by viewing the substrate or dispensing head.

9. A method according to claim 8 wherein the operating parameter is examined by viewing a fiducial mark on the dispensing head or substrate

10. A method according to claim 1 wherein:

the deposition apparatus includes a dispensing head with multiple nozzles to dispense fluid droplets containing the probes or probe precursors, and a transport system to move at least one of the dispensing head and substrate relative to the other as the droplets are dispensed from the head, so as to form the array;

the drive pattern controls operation of the transport system;

the operating parameter is the position of the substrate or dispensing head, or orientation of a nozzle, and is examined by viewing the substrate, dispensing head, or nozzle, or a droplet pattern previously dispensed from the head.

11. A method according to claim 7 additionally comprising saving the target drive pattern in a memory of the deposition apparatus, and wherein the corrected drive pattern is saved in the memory, prior to operating the dispensing head and transport system to form the array.

12. A method according to claim 7 additionally comprising saving the target drive pattern in a memory of the deposition apparatus, and wherein the corrected drive pattern is derived by modifying, based on the detected error, instructions to at least one deposition apparatus component based on the target drive pattern during operation of the dispensing head and transport system to form the array.

13. A method according to claim 1 wherein the at least one parameter is the position of the substrate in the deposition apparatus.

14. A method according to claim 7 wherein the at least one parameter is a position of the dispensing head.

15. (AMENDED) A method according to claim 7 wherein the deposition apparatus further includes a position encoder to detect the position of the dispensing head or the substrate, and wherein the at least one parameter is ~~the~~ an accuracy of the encoder.

16. A method according to claim 7 wherein the at least one parameter is the accuracy in an ability of the transport system to move the substrate to an expected location in response to a command.

17. A method according to claim 7 wherein the dispensing head has multiple droplet dispensing nozzles, and wherein the at least one parameter is a position of a nozzle.

18. (AMENDED) A method of fabricating an addressable array of biopolymer probes on a substrate according to a target array pattern using a deposition apparatus

which, when operated according to a target drive pattern based on nominal operating parameters of the apparatus and which is stored in a memory of the deposition apparatus, provides the probes on the substrate in the target array pattern, the method comprising:

when an error from a nominal value exists in at least one operating parameter, which error will result in use of the target drive pattern producing a discrepancy between the target array pattern and an actual array pattern deposited then deriving, based on the error, a corrected drive pattern from the target drive pattern such that use of the corrected drive pattern results in a reduced discrepancy between the target and actual array patterns; and

operating the deposition apparatus according to the corrected drive pattern so as to fabricate the array. .

19. A method according to claim 18 wherein the corrected drive pattern is saved in the memory.

46. (NEW) A method according to claim 1 wherein:

the deposition apparatus includes a dispensing head to dispense fluid droplets containing the probes or probe precursors, and a transport system to move at least one of the dispensing head and substrate relative to the other as the droplets are dispensed from the head, so as to form the array;

the drive pattern controls operation of the transport system; and

the at least one parameter is an accuracy in an ability of the transport system to move the substrate or head to an expected location in response to a command.

47. (NEW) A method according to claim 46 wherein the at least one operating parameter is a deviation of actual movement of the substrate or head from a corresponding nominal axis of movement.

48. (NEW) A method according to claim 46 wherein the at least one operating parameter is an accuracy in an ability of the transport system to move the substrate to an expected location in response to a command.

49. (NEW) A method according to claim 1 wherein the operating parameter is a fluid volume dispensed by the deposition apparatus.

50. (NEW) A method according to claim 1 wherein the operating parameter is an effect of thermal expansion.

51. (NEW) A method according to claim 1 wherein:

the deposition apparatus includes a dispensing head to dispense fluid droplets containing the probes or probe precursors, and a transport system to move at least one of the dispensing head and substrate relative to the other as the droplets are dispensed from the head, so as to form the array;

the apparatus further includes an encoder to provide data on the location of the substrate or head; and

the at least one operating parameter is an encoder error.

52. (NEW) A method according to claim 1 wherein:

the deposition apparatus includes a dispensing head with multiple nozzles to dispense fluid droplets containing the probes or probe precursors, and a transport system to move at least one of the dispensing head and substrate relative to the other as the droplets are dispensed from the head, so as to form the array;

the drive pattern controls operation of the transport system;

the operating parameter is the position of the dispensing head, or orientation of a nozzle, and is examined by viewing the dispensing head, or nozzle.

53. (NEW) A method according to claim 1 wherein the position is a dynamic position.

54. (NEW) A method according to claim 14 wherein the position is a dynamic position.

55. (NEW) A method according to claim 49 wherein the deposition apparatus comprises multiple jets for dispensing droplets, and wherein the corrected drive pattern comprises an instruction to switch to a different jet when a deviation from nominal volume is encountered for one jet which is more than a predetermined tolerance.